

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SIANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.

Connecting via Winsock to STN

Trying 3106016892...Open

Welcome to STN International! Enter x:x

LOGINID:sssptal623paz

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * Welcome to STN International * * * * *

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
NEWS 2 Sep 29 The Philippines Inventory of Chemicals and Chemical
Substances (PICCS) has been added to CHEMLIST
NEWS 3 Oct 27 New Extraction Code PAX now available in Derwent
Files
NEWS 4 Oct 27 SET ABBREVIATIONS and SET PLURALS extended in
Derwent World Patents Index files
NEWS 5 Oct 27 Patent Assignee Code Dictionary now available
in Derwent Patent Files
NEWS 6 Oct 27 Plasdoc Key Serials Dictionary and Echoing added to
Derwent Subscriber Files WPIDS and WPIX
NEWS 7 Nov 29 Derwent announces further increase in updates for DWPI
NEWS 8 Dec 5 French Multi-Disciplinary Database PASCAL Now on STN
NEWS 9 Dec 5 Trademarks on STN - New DEMAS and EUMAS Files
NEWS 10 Dec 15 2001 STN Pricing
NEWS 11 Dec 17 Merged CEABA-VTB for chemical engineering and
biotechnology
NEWS 12 Dec 17 Corrosion Abstracts on STN
NEWS 13 Dec 17 SYNTHLINE from Prouis Science now available on STN
NEWS 14 Dec 17 The CA Lexicon available in the CAPLUS and CA files
NEWS 15 Jan 05 AIDSLINE is being removed from STN
NEWS 16 Feb 06 Engineering Information Encompass files have new names
NEWS 17 Feb 16 TOXLINE no longer being updated

NEWS EXPRESS FREE UPGRADE 5.0e FOR STN EXPRESS 5.0 WITH DISCOVER!
(WINDOWS) NOW AVAILABLE
NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS INTER General Internet Information
NEWS LOGIN Welcome Banner and News Items
NEWS PHONE Direct Dial and Telecommunication Network Access to STN
NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

All use of STN is subject to the provisions of the STN Customer
agreement. Please note that this agreement limits use to scientific
research. Use for software development or design or implementation
of commercial gateways or other similar uses is prohibited and may
result in loss of user privileges and other penalties.

* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 07:24:59 ON 18 APR 2001

=> file reg

COST IN U.S. DOLLARS

SINCE FILE TOTAL
ENTRY SESSION

FULL ESTIMATED COST

0.15

0.15

FILE 'REGISTRY' ENTERED AT 07:25:09 ON 18 APR 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2001 American Chemical Society (ACS)

STRUCTURE FILE UPDATES: 17 APR 2001 HIGHEST RN 331714-48-8
DICTIONARY FILE UPDATES: 17 APR 2001 HIGHEST RN 331714-48-8

TSCA INFORMATION NOW CURRENT THROUGH July 8, 2000

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Structure search limits have been increased. See HELP SLIMIT
for details.

=> e neotame/cn

E1	1	NEOTALL F/CN
E2	1	NEOTALL G/CN
E3	1 -->	NEOTAME/CN
E4	1	NEOTAN UE 1402/CN
E5	1	NEOTAN UE 3100/CN
E6	1	NEOTARCHOCIN/CN
E7	1	NEOTEBANYL/CN
E8	1	NEOTEBEN/CN
E9	1	NEOTELOMYCIN/CN
E10	1	NEOTEMP/CN
E11	1	NEOTENINE/CN
E12	1	NEOTENONE/CN

=> s e3; d

L1 1 NEOTAME/CN

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2001 ACS

RN 165450-17-9 REGISTRY

CN L-Phenylalanine, N-(3,3-dimethylbutyl)-L-.alpha.-aspartyl-, 2-methyl
ester

(9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN L-Phenylalanine, N-[N-(3,3-dimethylbutyl)-L-.alpha.-aspartyl]-, 1-methyl
ester

OTHER NAMES:

CN **Neotame**

FS STEREOSEARCH

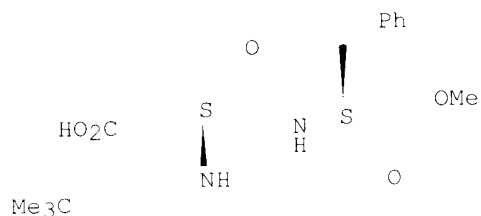
MF C20 H30 N2 O5

CI COM

SR CA

LC STN Files: AGRICOLA, ANABSTR, BIOSIS, CA, CAPLUS, CASREACT, CBNB, CIN,
MRCK*, PROMT, TOXLIT, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



59 REFERENCES IN FILE CA (1967 TO DATE)
 9 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 59 REFERENCES IN FILE CAPLUS (1967 TO DATE)

=> file caplus
 COST IN U.S. DOLLARS

SINCE FILE ENTRY	TOTAL SESSION
5.92	6.07

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 07:26:36 ON 18 APR 2001
 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
 COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications.

FILE COVERS 1967 - 18 Apr 2001 VOL 134 ISS 17
 FILE LAST UPDATED: 17 Apr 2001 (20010417/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

Now you can extend your author, patent assignee, patent information, and title searches back to 1907. The records from 1907-1966 now have this searchable data in CAOLD. You now have electronic access to all of CA: 1907 to 1966 in CAOLD and 1967 to the present in CAPLUS on STN.

The CA Lexicon is now available in the Controlled Term (/CT) field. Enter HELP LEXICON for full details.

Attention, the CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

=> s ll<neotame>

SmartSELECT INITIATED

New TRANSFER and ANALYZE Commands Now Available
 See HELP TRANSFER and HELP ANALYZE for Details

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.33

6.40

FILE 'REGISTRY' ENTERED AT 07:26:58 ON 18 APR 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2001 American Chemical Society (ACS)

SET SMARTSELECT ON

SET COMMAND COMPLETED

SEL L1 1- NEOTAME

'NEOTAME' IS NOT A VALID FIELD CODE FOR FILE 'REGISTRY'

The following are valid field codes:

AF ----- Alternate Molecular Formula
AR ----- Alternate Registry Number
CCI ----- Component Substance Class Identifier
CHEM ----- CAS Registry Numbers and Selected Names
CI ----- Substance Class Identifier
CMF ----- Component Molecular Formulas
CN ----- Chemical Names (Up to 50)
CRN ----- Component Registry Numbers
DEF ----- Definition
DR ----- Deleted Registry Number
EA ----- Elemental Analysis for Ring System
ES ----- Elemental Sequence for Ring System
FCN ----- All Chemical Names
FS ----- File Segment
IN ----- CA Index Name
LC ----- CAS Registry Number Locator
MF ----- Molecular Formula
NAME ----- Selected Substance Names
PCT ----- Polymer Class Term
PR ----- Preferred Registry Number
RF ----- Ring System Formula
RID ----- Ring Identifier
RN ----- CAS Registry Number
RR ----- Replacing Registry Number
SCN ----- Short Chemical Name (IN and OTHER NAMES)
SEQ ----- Protein Sequence Display using 1 Letter Amino Acid Codes (default)
SEQ3 ----- Protein Sequence Display using 3 Letter Amino Acid Codes
SQEFP --- Protein Sequence (exact family search form)
SQEN ---- Nucleic Acid Sequence (exact search form)
SQEP ---- Protein Sequence (exact search form)
SQSFP --- Protein Sequence (subsequence family search form)
SQSN ---- Nucleic Acid Sequence (subsequence search form)
SQSP ---- Protein Sequence (subsequence search form)
SR ----- Source of Registration
SZ ----- Size for Ring System
ENTER DISPLAY CODE (CHEM) OR ?:chem
L2 SEL L1 1- CHEM : 2 TERMS

SET SMARTSELECT OFF

SET COMMAND COMPLETED

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

9.11

15.51

FILE 'CAPLUS' ENTERED AT 07:27:27 ON 18 APR 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY (ACS)

S L2

L3 64 L2

=> d scan 13

L3 64 ANSWERS CAPLUS COPYRIGHT 2001 ACS
IC ICM C07C229-28
ICS C07D279-04; C07D275-06; C07D315-00
NCL 560039000
CC 17-6 (Food and Feed Chemistry)
TI N-[n-(3,3-dimethylbutyl)-L-.alpha.-aspartyl]-L-phenylalanine 1-methyl
ester synergistic sweetener blends
ST sweetening agent synergy dipeptide deriv; aspartame deriv sweetener
synergy; **neotame** sweetener synergy
IT Sweetening agents
(N-[n-(3,3-dimethylbutyl)-l-.alpha.-aspartyl]-l-phenylalanine 1-Me
ester synergistic sweetener blends)
IT Cooperative phenomena
(synergism; N-[n-(3,3-dimethylbutyl)-L-.alpha.-aspartyl]-L-
phenylalanine 1-Me ester synergistic sweetener blends)
IT 57-50-1, Sucrose, biological studies 81-07-2, Saccharin 22839-47-0,
Aspartame 55589-62-3, Acesulfamepotassium **165450-17-9**,
Neotame
RL: BAC (Biological activity or effector, except adverse); FFD (Food or
feed use); BIOL (Biological study); USES (Uses)
(N-[n-(3,3-dimethylbutyl)-L-.alpha.-aspartyl]-L-phenylalanine 1-Me
ester synergistic sweetener blends)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):4

L3 64 ANSWERS CAPLUS COPYRIGHT 2001 ACS
IC ICM C07C229-00
NCL 560040000
CC 34-3 (Amino Acids, Peptides, and Proteins)
TI Method for preparing and purifying an N-alkylated aspartame derivative
ST aspartame dimethylbutyl prepn purifn
IT **165450-17-9P**
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP
(Preparation)
(prepn. and purifn. of N-alkylated aspartame deriv.)
IT 2987-16-8, 3,3-Dimethylbutyraldehyde 22839-47-0, Aspartame
RL: RCT (Reactant)
(prepn. and purifn. of N-alkylated aspartame deriv.)

L3 64 ANSWERS CAPLUS COPYRIGHT 2001 ACS
CC 17-0 (Food and Feed Chemistry)
TI **Neotame**: discovery, properties, utility
ST review **neotame** sweetener property use
IT Sweetening agents
(noncariogenic, noncaloric, nonnutritive; **Neotame** discovery,
properties, and utility as)
IT **165450-17-9, Neotame**
RL: BAC (Biological activity or effector, except adverse); FFD (Food or
feed use); PRP (Properties); BIOL (Biological study); USES (Uses)

(discovery, properties, and utility as sweetener)

L3 64 ANSWERS CAPLUS COPYRIGHT 2001 ACS
IC ICM A23L001-236
ICS A23L001-22; C07K005-075
CC 17-6 (Food and Feed Chemistry)
TI Sweetener for improving taste
ST aspartame acesulfame amino acid deriv sweetener
IT Sweetening agents
(contg. aspartame and acesulfame K and amino acid deriv.)
IT Beverages
(contg. aspartame and acesulfame K and amino acid deriv. as sweetener)
IT **165450-17-9**
RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)
(sweetener contg. aspartame and acesulfame K and)
IT 22839-47-0, Aspartame 33665-90-6, Acesulfame
RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)
(sweetener contg. aspartame and acesulfame K and amino acid deriv.)

L3 64 ANSWERS CAPLUS COPYRIGHT 2001 ACS
IC ICM C07K005-075
CC 17-1 (Food and Feed Chemistry)
TI Crystallization processes of stable crystals of aspartame derivatives
ST crystn aspartame deriv sweetener
IT **165450-17-9 165450-17-9D**, derivs.
RL: FFD (Food or feed use); BIOL (Biological study); USES (Uses)
(crystn. of stable aspartame)
IT 67-56-1, Methanol, uses
RL: NUU (Nonbiological use, unclassified); USES (Uses)
(in crystn. of stable aspartame)

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):0

=> d his

(FILE 'HOME' ENTERED AT 07:24:59 ON 18 APR 2001)

FILE 'REGISTRY' ENTERED AT 07:25:09 ON 18 APR 2001
E NEOTAME/CN

L1 1 S E3

FILE 'CAPLUS' ENTERED AT 07:26:36 ON 18 APR 2001

FILE 'REGISTRY' ENTERED AT 07:26:58 ON 18 APR 2001
SET SMARTSELECT ON
L2 SEL L1 1- CHEM : 2 TERMS
SET SMARTSELECT OFF

FILE 'CAPLUS' ENTERED AT 07:27:27 ON 18 APR 2001

L3 64 S L2

=> s anhydrous(1)L3

6392 ANHYDROUS
L4 0 ANHYDROUS(L)L3

=> s dry (1) L3

234680 DRY
930 DRIES
23 DRYs
235429 DRY
(DRY OR DRIES OR DRYs)

L5 3 DRY (L) L3

=> d 15 1-3 ti

L5 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2001 ACS

TI Neotame: discovery, properties, utility

L5 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2001 ACS

TI The use of cyclodextrin to stabilize N-[N-(3,3-dimethylbutyl)-L-.alpha.-aspartyl]-L-phenylalanine 1-methyl ester

L5 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2001 ACS

TI Neotame sweetener for dairy products and dairy product substitutes

=> d 15 1-3 ti fbib abs

L5 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2001 ACS

TI Neotame: discovery, properties, utility

AN 2000:256584 CAPLUS

DN 133:16459

TI Neotame: discovery, properties, utility

AU Nofre, Claude; Tinti, Jean-Marie

CS Lyon, F-69008, Fr.

SO Food Chem. (2000), 69(3), 245-257

CODEN: FOCHDJ; ISSN: 0308-8146

PB Elsevier Science Ltd.

DT Journal; General Review

LA English

AB A review with 39 refs. **Neotame** (NTM) is a new nonnutritive sweetener. NTM is a deriv. of aspartame (APM). NTM has a clean sweet taste and a good flavor profile. It is a high-potency sweetener: it is 6000-10,000 times sweeter than sucrose and 30-60 times sweeter than APM. NTM is a noncaloric, noncariogenic sweetener. NTM has an extensive shelf life in **dry** conditions. In aq. food systems, it presents the same functionalities as APM in acidic medium, but it is significantly

more

stable in neutral medium. Consequently, NTM should be a useful sweetener in baked goods. NTM is compatible with reducing sugars and

aldehyde-based

flavoring agents. It has flavor-enhancing properties. Its relative cost is expected to be lower than sucrose or APM at sweetness equivalence. A petition was filed in the USA in Dec. 1998 for its approval as a general-use sweetener; other regulatory activities are underway in

several

countries.

RE.CNT 39

RE

(3) Beck, C; Low calorie and special dietary foods 1978, P59 CAPLUS

(7) Homler, B; Aspartame: physiology and biochemistry 1984, P247 CAPLUS

(8) Ketelsen, S; Journal of Food Science 1993, V58, P1418 CAPLUS

(10) Lindinger, W; Alcoholism Clinical and Experimental Research 1997, V21, P939 CAPLUS

(13) Mazur, R; Developments in sweeteners 1979, P125 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2001 ACS

TI The use of cyclodextrin to stabilize N-[N-(3,3-dimethylbutyl)-L-.alpha.-aspartyl]-L-phenylalanine 1-methyl ester

AN 2000:190872 CAPLUS

DN 132:221731

TI The use of cyclodextrin to stabilize N-[N-(3,3-dimethylbutyl)-L-.alpha.-aspartyl]-L-phenylalanine 1-methyl ester
 IN Bishay, Ihab E.; Fotos, Jim G.; Desai, Nitin; Cleary, Michael; Schroeder, Steve
 PA The Nutrasweet Company, USA
 SO PCT Int. Appl., 42 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000015049	A1	20000323	WO 1999-US21471	19990916
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
				US 1998-100867	19980917
	AU 9961504	A1	20000403	AU 1999-61504	19990916
				US 1998-100867	19980917
				WO 1999-US21471	19990916

AB N-[N-(3,3-Dimethylbutyl)-L-.alpha.-aspartyl]-L-phenylalanine 1-Me ester (**neotame** sweetener) is combined with cyclodextrin to form compns. exhibiting increased stability and soly. The cyclodextrin may be .alpha., .beta. or .gamma., or a mixt. of these, and may be substituted or unsubstituted. This stabilized complex can be used in a variety of applications. Thus, a carbonated cola contains 1.632 g cyclodextrin-**neotame** complex (5:1) in 977 g water, plus other ingredients. Complex formation can be accomplished by a variety of methods, such as co-pptn., slurry complexation, paste complexation, mixing and heating, extrusion, **dry** mixing, wet pelletization, agglomeration and other methods.

RE.CNT 3

RE

- (1) Majid; US 5070081 A 1991 CAPLUS
- (2) Nofre; US 5480668 A 1996 CAPLUS
- (3) Ojima; EP 0097950 A 1984 CAPLUS

L5 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2001 ACS

TI Neotame sweetener for dairy products and dairy product substitutes

AN 1999:404813 CAPLUS

DN 131:31305

TI Neotame sweetener for dairy products and dairy product substitutes

IN Gaughan, Wanda M.; Gerlat, Paula A.; Ziegler, Jeanette G.; Walters, Gale C.; Logli, Lori; Corliss, Glenn; Finley, John

PA The Nutrasweet Company, USA

SO PCT Int. Appl., 57 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9930578	A1	19990624	WO 1998-US27176	19981217
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,			

DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG,
 KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
 NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
 UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
 CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9919364 A1 19990705 US 1997-69952 19971217
 AU 1999-19364 19981217
 US 1997-69952 19971217
 WO 1998-US27176 19981217

AB N-[N-(3,3-Dimethylbutyl)-L-.alpha.-aspartyl]-L-phenylalanine 1-Me ester (**neotame**) is used to sweeten dairy products, including milk (from various species and of various milk fat content), enzyme treated milk, filled milk, cream, creamers, cultured milk, milk concs., **dry** milk, fluid and dried whey, fluid and **dry** milk based desserts and beverages, and fluid and **dry** aerated desserts and toppings. The dairy products also include frozen cultured milk products, such as frozen yogurt, and frozen fluid dairy products, such as ice cream, ice milk, sherbet, custards and french ice cream, mellorine, novelties, and the like. Dairy analog products include soy milk, soy powder, caseinates, and non-dairy coffee whiteners, as well as frozen products such as sorbet and non-dairy novelties. Thus, an orange sherbet may be sweetened with

20

ppm **neotame**.

RE.CNT 6

RE

- (1) Ajinomoto; WO 9839979 A 1998 CAPLUS
- (2) Ajinomoto; WO 9839979 A 1998 CAPLUS
- (3) Nofre, C; WO 9530689 A 1995 CAPLUS
- (4) Nofre, C; US 5480668 A 1996 CAPLUS
- (5) Oshawa Group; CA 1267030 A 1990

ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> logoff hold

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
15.18	30.69

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
-1.76	-1.76

CA SUBSCRIBER PRICE

SESSION WILL BE HELD FOR 60 MINUTES

STN INTERNATIONAL SESSION SUSPENDED AT 07:30:30 ON 18 APR 2001

Connecting via Winsock to STN

Trying 3106016892...Open

Welcome to STN International! Enter x:x

LOGINID:sssptal623paz

PASSWORD:

* * * * * RECONNECTED TO STN INTERNATIONAL * * * * *
 SESSION RESUMED IN FILE 'CAPLUS' AT 07:53:26 ON 18 APR 2001
 FILE 'CAPLUS' ENTERED AT 07:53:26 ON 18 APR 2001
 COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY (ACS)

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
------------	-------

FULL ESTIMATED COST	ENTRY 15.18	SESSION 30.69
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.76	-1.76

=> d his

(FILE 'HOME' ENTERED AT 07:24:59 ON 18 APR 2001)

FILE 'REGISTRY' ENTERED AT 07:25:09 ON 18 APR 2001
E NEOTAME/CN

L1 1 S E3

FILE 'CAPLUS' ENTERED AT 07:26:36 ON 18 APR 2001

FILE 'REGISTRY' ENTERED AT 07:26:58 ON 18 APR 2001

L2 SET SMARTSELECT ON
SEL L1 1- CHEM : 2 TERMS
SET SMARTSELECT OFF

FILE 'CAPLUS' ENTERED AT 07:27:27 ON 18 APR 2001

L3 64 S L2
L4 0 S ANHYDROUS(L) L3
L5 3 S DRY (L) L3

=> s l3 and stability

436415 STABILITY
17851 STABILITIES
445166 STABILITY
(STABILITY OR STABILITIES)

L6 7 L3 AND STABILITY

=> d l6 1-7 ti

L6 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2001 ACS
TI Structure, Dynamics, and **Stability** of .beta.-Cyclodextrin
Inclusion Complexes of Aspartame and **Neotame**

L6 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2001 ACS
TI Cereals and cereal-based food sweetened with **neotame**

L6 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2001 ACS
TI Method for preparing crystal of aspartame derivative excellent in
stability

L6 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2001 ACS
TI Discovery and development of **neotame**

L6 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2001 ACS
TI The use of cyclodextrin to stabilize N-[N-(3,3-dimethylbutyl)-L-.alpha.-
aspartyl]-L-phenylalanine 1-methyl ester

L6 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2001 ACS
TI Low-calorie granular sweeteners containing dextrin with high dietary
fiber content

L6 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2001 ACS
TI New dipeptide derivatives and analogs useful as sweetening agents, and

process for their preparation

=> d 16 3,4,7 ti fbib abs

L6 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2001 ACS
TI Method for preparing crystal of aspartame derivative excellent in
stability
AN 2000:314716 CAPLUS
DN 132:321238
TI Method for preparing crystal of aspartame derivative excellent in
stability
IN Kawahara, Shigeru; Kishishita, Akihiro; Nagashima, Kazutaka; Takemoto,
Tadashi
PA Ajinomoto Co., Inc., Japan
SO PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
PI WO 2000026235	A1	20000511	WO 1999-JP6083	19991101
W: BR, CA, CN, HU, JP, KR, MX, RU, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
			JP 1998-310227	19981030
			JP 1998-310228	19981030
JP 2000136198	A2	20000516	JP 1998-310228	19981030
AB	A method for prepg. the A type crystal of N-(3,3-dimethylbutyl)-APM being excellent in stability , comprises holding the B type crystal thereof under a controlled condition with an abs. humidity of 0.203 kg/kg or lower and a material temp. of 25.degree. to 80.degree., to thereby produce crystal transition, including a method for prepg. the A type crystal of N-(3,3-dimethylbutyl)-APM. holding the D type crystal thereof under a controlled condition with an abs. humidity of 0.0550 kg/kg or lower and a material temp. of 25.degree. to 80.degree., to thereby causing crystal transition. These crystal transition methods allow the prepn. of a crystal excellent in stability in a cost-effective manner.			

RE.CNT 15
RE
(1) Ajinomoto Co Inc; JP 02243699 A CAPLUS
(2) Ajinomoto Co Inc; US 5543544 A CAPLUS
(4) Ajinomoto Co Inc; EP 362706 A1 1990 CAPLUS
(7) Nofre Claude; FR 2719590 A CAPLUS
(8) Nofre Claude; FR 2719591 A CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2001 ACS
TI Discovery and development of **neotame**
AN 2000:250511 CAPLUS
DN 132:292833
TI Discovery and development of **neotame**
AU Witt, John
CS Nutrition and Consumer Sector, Monsanto Company, Mt. Prospect, IL, USA
SO World Rev. Nutr. Diet. (1999), 85(Low-Calorie Sweeteners), 52-57
CODEN: WRNDAT; ISSN: 0084-2230
PB S. Karger AG
DT Journal; General Review
LA English

AB A review without refs., describing development and characterization of **neotame**, sweetness potency and flavor profile of **neotame** in water, and application, functionality, and sweetness level and **stability** of **neotame**.

L6 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2001 ACS

TI New dipeptide derivatives and analogs useful as sweetening agents, and process for their preparation

AN 1995:701729 CAPLUS

DN 123:84006

TI New dipeptide derivatives and analogs useful as sweetening agents, and process for their preparation

IN Nofre, Claude; Tinti, Jean Marie

PA Fr.

SO Fr. Demande, 23 pp.

CODEN: FRXXBL

DT Patent

LA French

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	FR 2697844	A1	19940513	FR 1992-13615	19921112
	FR 2697844	B1	19950127		
	US 5480668	A	19960102	US 1993-149365	19931109
				FR 1992-13615	19921112
	CA 2139233	AA	19940526	CA 1993-2139233	19931110
				FR 1992-13615	19921112
	WO 9411391	A1	19940526	WO 1993-FR1103	19931110
	W: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KP, KR, KZ, LK, LV, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, UZ, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
				FR 1992-13615	19921112
	AU 9454681	A1	19940608	AU 1994-54681	19931110
	AU 664663	B2	19951123		
				FR 1992-13615	19921112
				WO 1993-FR1103	19931110
	LT 3142	B	19950131	LT 1993-1457	19931110
				FR 1992-13615	19921112
	EP 669935	A1	19950906	EP 1994-900182	19931110
	EP 669935	B1	19960605		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT,				
SE				FR 1992-13615	19921112
				WO 1993-FR1103	19931110
	HU 72192	A2	19960328	HU 1994-3842	19931110
	HU 218158	B	20000628		
				FR 1992-13615	19921112
	JP 08503206	T2	19960409	JP 1993-511787	19931110
				FR 1992-13615	19921112
				WO 1993-FR1103	19931110
	AT 138935	E	19960615	AT 1994-900182	19931110
				FR 1992-13615	19921112
	ES 2091114	T3	19961016	ES 1994-900182	19931110
				FR 1992-13615	19921112
	RO 112621	B1	19971128	RO 1994-2023	19931110
				FR 1992-13615	19921112
				WO 1993-FR1103	19931110
	RU 2107071	C1	19980320	RU 1994-46457	19931110
				FR 1992-13615	19921112
				WO 1993-FR1103	19931110

IL 107551	A1	19980816	IL 1993-107551	19931110
			FR 1992-13615	19921112
CZ 285018	B6	19990512	CZ 1994-3319	19931110
			FR 1992-13615	19921112
SK 280180	B6	19990910	SK 1994-1586	19931110
			FR 1992-13615	19921112
			WO 1993-FR1103	19931110
PL 177090	B1	19990930	PL 1993-306841	19931110
			FR 1992-13615	19921112
			WO 1993-FR1103	19931110
ZA 9308430	A	19940613	ZA 1993-8430	19931111
			FR 1992-13615	19921112
CN 1090571	A	19940810	CN 1993-114462	19931112
CN 1038747	B	19980617		
			FR 1992-13615	19921112
FI 9405451	A	19941222	FI 1994-5451	19941121
			FR 1992-13615	19921112
			WO 1993-FR1103	19931110
NO 9405090	A	19941230	NO 1994-5090	19941230
			FR 1992-13615	19921112
			WO 1993-FR1103	19931110

OS CASREACT 123:84006; MARPAT 123:84006
 GI For diagram(s), see printed CA Issue.
 AB Title compds. I [R = C4-13 (un)satd. (a)cyclic hydrocarbyl; n = 1 or 2; Y = CO2Me, CO2Et, Me, CH2OH, CONMe2, Ph, 2-furyl, H; Z = CH2Ph, Ph, Bu, CO2Me, CO2Et, CO2Pr, fenchyloxycarbonyl, CONHR'; R' = Me, Et, Pr, isoamyl, CHMeCO2Me, dicyclopropylmethyl, 2,2,4,4-tetramethyl-3-thietanyl, etc.]
 are
 claimed, and are useful as sweeteners. I include aspartame (II) derivs., and show both higher sweetening power and increased **stability** vs. II. For example, reductive alkylation of aspartame by com. Me3CCH2CHO and NaBH3CN in MeOH at room temp. gave 62% title compd. III. Tested as aq. solns., the sweetening power of III was approx. 80-fold that of II. Also, in aq. soln. at pH 3 and 70.degree., the half-life of III was 55 h, vs. 24 h for II. Sweetening and/or **stability** data for some of the other claimed I are also reported.

=>		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	27.77	43.28
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-3.53	-3.53

FILE 'STNGUIDE' ENTERED AT 07:58:29 ON 18 APR 2001
 USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
 COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY, JAPAN SCIENCE
 AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
 LAST RELOADED: Apr 13, 2001 (20010413/UP).

=>		
NAME	CREATED	NOTES/TITLE
-----	-----	-----
AMINOPOLY/A	16 APR 2001	23i ANSWERS IN FILE CAPLUS

TWOAMINOPOLY/Q 16 APR 2001 UPLOADED STRUCTURE

=>

NO SAVED SDI REQUESTS

=>

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	0.00	43.28
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	-3.53

FILE 'CAPLUS' ENTERED AT 07:58:49 ON 18 APR 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications.

FILE COVERS 1967 - 18 Apr 2001 VOL 134 ISS 17
FILE LAST UPDATED: 17 Apr 2001 (20010417/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

Now you can extend your author, patent assignee, patent information, and title searches back to 1907. The records from 1907-1966 now have this searchable data in CAOLD. You now have electronic access to all of CA: 1907 to 1966 in CAOLD and 1967 to the present in CAPLUS on STN.

The CA Lexicon is now available in the Controlled Term (/CT) field. Enter HELP LEXICON for full details.

Attention, the CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

=>

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	0.33	43.61
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	-3.53

FILE 'STNGUIDE' ENTERED AT 07:58:56 ON 18 APR 2001

USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY, JAPAN SCIENCE
AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Apr 13, 2001 (20010413/UP).

=>

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	0.00	43.61
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	-3.53

FILE 'CAPLUS' ENTERED AT 07:59:41 ON 18 APR 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications.

FILE COVERS 1967 - 18 Apr 2001 VOL 134 ISS 17
FILE LAST UPDATED: 17 Apr 2001 (20010417/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REGISTRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

Now you can extend your author, patent assignee, patent information, and title searches back to 1907. The records from 1907-1966 now have this searchable data in CAOLD. You now have electronic access to all of CA: 1907 to 1966 in CAOLD and 1967 to the present in CAPLUS on STN.

The CA Lexicon is now available in the Controlled Term (/CT) field. Enter HELP LEXICON for full details.

Attention, the CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

=>

ANSWER SET L3 HAS BEEN SAVED AS 'NEOTAME/A'

=> logoff hold

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	0.33	43.94
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION

CA SUBSCRIBER PRICE 0.00 -3.53

SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 08:00:12 ON 18 APR 2001

Connecting via Winsock to STN

Trying 3106016892...Open

Welcome to STN International! Enter x:x

LOGINID:sssptal623paz

PASSWORD:

* * * * * RECONNECTED TO STN INTERNATIONAL * * * * *
SESSION RESUMED IN FILE 'CAPLUS' AT 08:02:19 ON 18 APR 2001
FILE 'CAPLUS' ENTERED AT 08:02:19 ON 18 APR 2001
COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY (ACS)

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.33	43.94
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-3.53

=> d his

(FILE 'HOME' ENTERED AT 07:24:59 ON 18 APR 2001)

FILE 'REGISTRY' ENTERED AT 07:25:09 ON 18 APR 2001

E NEOTAME/CN

L1 1 S E3

FILE 'CAPLUS' ENTERED AT 07:26:36 ON 18 APR 2001

FILE 'REGISTRY' ENTERED AT 07:26:58 ON 18 APR 2001

SET SMARTSELECT ON

L2 SEL L1 1- CHEM : 2 TERMS

SET SMARTSELECT OFF

FILE 'CAPLUS' ENTERED AT 07:27:27 ON 18 APR 2001

L3 64 S L2

L4 0 S ANHYDROUS(L) L3

L5 3 S DRY (L) L3

L6 7 S L3 AND STABILITY

FILE 'STNGUIDE' ENTERED AT 07:58:29 ON 18 APR 2001

FILE 'CAPLUS' ENTERED AT 07:58:49 ON 18 APR 2001

FILE 'STNGUIDE' ENTERED AT 07:58:56 ON 18 APR 2001

FILE 'CAPLUS' ENTERED AT 07:59:41 ON 18 APR 2001

SAVE L3 NEOTAME/A

=> s L3 and polycrystal?

29723 POLYCRYSTAL?

L7 0 L3 AND POLYCRYSTAL?

=> s amorphous (1) l3

175190 AMORPHOUS

L8 2 AMORPHOUS (L) L3

=> d 18 1-2 ti fbib abs

L8 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2001 ACS
TI Amorphous N-[N-(3,3-dimethylbutyl)-L-.alpha.-aspartyl]-L-phenylalanine
1-methyl ester
AN 2000:368409 CAPLUS
DN 133:4999
TI Amorphous N-[N-(3,3-dimethylbutyl)-L-.alpha.-aspartyl]-L-phenylalanine
1-methyl ester
IN Schroeder, Steve A.; Wang, Run
PA The Nutrasweet Company, USA
SO PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	---	-----	-----	-----
PI	WO 2000031118	A1	20000602	WO 1999-US27363	19991119
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
				US 1998-109391	19981120

AB **Amorphous** N-[N-(3,3-dimethylbutyl)-L-.alpha.-aspartyl]-L-phenylalanine 1-Me ester (the sweetener **neotame**) was prepd. by a process comprising melting and then cooling the melt. Thus, **neotame** was heated slowly past its m.p. of about 82.degree. until a temp. of about 92.degree. was reached. The **neotame** was then cooled to room temp. and ground to a cryst. powder. **Amorphous neotame** has improved soly. and dissoln. properties compared to the known monohydrate.

RE.CNT 3

RE

- (1) Leung, S; JOURNAL OF PHARMACEUTICAL SCIENCES 1998, V87(4), P508 CAPLUS
- (2) Padden, B; ANALYTICAL CHEMISTRY 1999, V71(16), P3325 CAPLUS
- (3) Prakash; US 5728862 A 1998 CAPLUS

L8 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2001 ACS
TI Crystal structure and physical characterization of neotame methanol solvate
AN 2000:258873 CAPLUS
DN 133:59068
TI Crystal structure and physical characterization of neotame methanol solvate
AU Dong, Zedong; Young, Victor G., Jr.; Padden, Brian E.; Schroeder, Steve A.; Prakash, Indra; Munson, Eric J.; Grant, David J. W.
CS Department of Pharmaceutics, College of Pharmacy, University of Minnesota,
Minneapolis, MN, 55455-0343, USA
SO J. Chem. Crystallogr. (1999), 29(8), 967-975
CODEN: JCCYEV; ISSN: 1074-1542
PB Kluwer Academic/Plenum Publishers
DT Journal

LA English
 AB The crystal structure of the methanol solvate (empirical formula:
 2C20H30N2O5.cntdot.3MeOH) of the dipeptide sweetener **neotame**,
 N-(3,3-dimethylbutyl)-L-.alpha.-aspartyl-L-phenylalanine Me ester, was
 detd. [a = 9.8989(1), b = 18.1331(1), c = 27.5725(1) .ANG., orthorhombic,
 space group P212121, Z = 4]. Each unit cell includes 8 **neotame**
 and 12 MeOH mols. Disorder exists in one **neotame** mol. and one
 MeOH mol. The crystals were characterized by the following techniques:
 hot-stage microscopy (HSM), Karl-Fischer titrimetry (KFT), powder x-ray
 diffractometry (PXRD), differential scanning calorimetry (DSC),
 thermogravimetry (TGA), and 13C solid-state NMR (SSNMR). Under HSM at a
 heating rate of 10.degree./min, the sample melts at 64-84.degree. and
 liberates bubbles at 71-86.degree.. DSC in open pans shows two
 overlapping endotherms at 56 and 71.degree., probably due to melting and
 desolvation, resp. TGA in open pans shows 5.9% wt. loss due to
 desolvation below 70.degree.. Under 23 mmHg over P4010 at 23.degree.,

the
 MeOH solvate produces pure **amorphous** anhydrate, which converts
 to cryst. **neotame**.H2O in the presence of moisture.

RE.CNT 21

RE

(1) Andrew, E; Prog NMR Spec 1971, V8, P1 CAPLUS
 (3) Anon; US 5728862 CAPLUS
 (5) Blessing, R; Acta Crystallogr 1995, VA51, P33 CAPLUS
 (6) Dixon, W; J Magn Res 1982, V49, P341 CAPLUS
 (7) Goodman, M; J Peptide Sci 1998, V4, P229 CAPLUS
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> logoff hold

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	10.06	53.67
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-1.18	-4.71

SESSION WILL BE HELD FOR 60 MINUTES
 STN INTERNATIONAL SESSION SUSPENDED AT 08:06:13 ON 18 APR 2001

Connecting via Winsock to STN

Trying 3106016892...Open

Welcome to STN International! Enter x:x

LOGINID:sssptal623paz

PASSWORD:

* * * * * RECONNECTED TO STN INTERNATIONAL * * * * *
 SESSION RESUMED IN FILE 'CAPLUS' AT 08:47:24 ON 18 APR 2001
 FILE 'CAPLUS' ENTERED AT 08:47:24 ON 18 APR 2001
 COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY (ACS)

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	10.06	53.67
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-1.18	-4.71

=> d his

(FILE 'HOME' ENTERED AT 07:24:59 ON 18 APR 2001)

FILE 'REGISTRY' ENTERED AT 07:25:09 ON 18 APR 2001
E NEOTAME/CN

L1 1 S E3

FILE 'CAPLUS' ENTERED AT 07:26:36 ON 18 APR 2001

FILE 'REGISTRY' ENTERED AT 07:26:58 ON 18 APR 2001
SET SMARTSELECT ON

L2 SEL L1 1- CHEM : 2 TERMS
SET SMARTSELECT OFF

FILE 'CAPLUS' ENTERED AT 07:27:27 ON 18 APR 2001

L3 64 S L2
L4 0 S ANHYDROUS(L) L3
L5 3 S DRY (L) L3
L6 7 S L3 AND STABILITY

FILE 'STNGUIDE' ENTERED AT 07:58:29 ON 18 APR 2001

FILE 'CAPLUS' ENTERED AT 07:58:49 ON 18 APR 2001

FILE 'STNGUIDE' ENTERED AT 07:58:56 ON 18 APR 2001

FILE 'CAPLUS' ENTERED AT 07:59:41 ON 18 APR 2001
SAVE L3 NEOTAME/A

L7 0 S L3 AND POLYCRYSTAL?
L8 2 S AMORPHOUS (L) L3

=> s l3 and anhydrate

326 ANHYDRATE
35 ANHYDRATES
353 ANHYDRATE
(ANHYDRATE OR ANHYDRATES)

L9 2 L3 AND ANHYDRATE

=> d l9 1-2 ti fbib abs

L9 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2001 ACS
TI Investigation of Polymorphism in Aspartame and **Neotame** Using
Solid-State NMR Spectroscopy
AN 2000:620337 CAPLUS
DN 133:349355
TI Investigation of Polymorphism in Aspartame and **Neotame** Using
Solid-State NMR Spectroscopy
AU Zell, M. T.; Padden, B. E.; Grant, D. J. W.; Schroeder, S. A.;
Wachholder,
K. L.; Prakash, I.; Munson, E. J.
CS Department of Chemistry, University of Minnesota, Minneapolis, MN, 55455,
USA
SO Tetrahedron (2000), 56(36), 6603-6616
CODEN: TETRAB; ISSN: 0040-4020
PB Elsevier Science Ltd.
DT Journal
LA English
AB We have been studying the artificial sweeteners aspartame
(l-aspartyl-l-phenylalanine Me ester) and **neotame**
(N-(3,3-dimethylbutyl)-l-aspartyl-l-phenylalanine Me ester) as compds.

which exhibit polymorphism. ¹³C CP/MAS NMR shows that aspartame exists in three distinct forms at room temp., depending on prepn. conditions. For two of the forms, there exists three resonances for each carbon, indicating three crystallog. inequivalent sites and therefore three distinct conformations and/or arrangements of aspartame mols. within the unit cell. Two-dimensional exchange spectroscopy using high-speed MAS and very high-power ¹H decoupling on uniformly ¹³C labeled aspartame is a very powerful tool for unambiguously assigning each resonance in the NMR spectrum of aspartame. Even for forms of aspartame that possesses multiple crystallog. inequivalent sites, it is possible to identify connectivities between the nuclei of each conformation and/or arrangement of mols. using two-dimensional NMR techniques. ¹³C CP/MAS NMR also shows that **neotame** exists in multiple solid forms. The most stable form of **neotame** under ambient conditions is a monohydrate. However, other forms can be prepd. by heating or using reduced pressures. High-speed magic-angle spinning can cause a change in polymorphic forms. Three different forms were produced upon spinning at 29 kHz for several days. The monohydrate was identified as the second form produced. Also, altering the crystn. and drying conditions can generate mixts. of the solid forms of **neotame**. When the monohydrate form of **neotame** was heated under vacuum, a mixt. of **anhydrate** forms was produced. In the reconversion to the monohydrate upon exposure to moisture under ambient conditions no significant changes were obsd. in the powder X-ray diffraction patterns during part of the reconversion process. This suggests that no change in form had occurred. The ¹³C CP/MAS NMR spectra, however, indicated the presence of many forms of **neotame** during the reconversion. One possible reason that solid-state NMR spectroscopy detected the changes in forms and powder X-ray diffraction did not is that the conformation of the **neotame** mols. changes between forms but the unit cell parameters do not change significantly.

RE.CNT 47

RE

- (1) Andrew, E; Prog NMR Spectrosc 1971, V8, P1 CAPLUS
 - (2) Anon; US 5510508 CAPLUS
 - (3) Anon; US 5728862 CAPLUS
 - (4) Anwar, J; J Pharm Sci 1989, V78, P337 CAPLUS
 - (5) Bennett, A; J Chem Phys 1992, V96, P8624 CAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2001 ACS
 TI Crystal structure and physical characterization of **neotame**
 methanol solvate
 AN 2000:258873 CAPLUS
 DN 133:59068
 TI Crystal structure and physical characterization of **neotame**
 methanol solvate
 AU Dong, Zedong; Young, Victor G., Jr.; Padden, Brian E.; Schroeder, Steve
 A.; Prakash, Indra; Munson, Eric J.; Grant, David J. W.
 CS Department of Pharmaceutics, College of Pharmacy, University of
 Minnesota,
 Minneapolis, MN, 55455-0343, USA
 SO J. Chem. Crystallogr. (1999), 29(8), 967-975
 CODEN: JCCYEV; ISSN: 1074-1542
 PB Kluwer Academic/Plenum Publishers
 DT Journal
 LA English
 AB The crystal structure of the methanol solvate (empirical formula:
 2C20H30N2O5.cntdot.3MeOH) of the dipeptide sweetener **neotame**,

N-(3,3-dimethylbutyl)-L-.alpha.-aspartyl-L-phenylalanine Me ester, was detd. [a = 9.8989(1), b = 18.1331(1), c = 27.5725(1) .ANG., orthorhombic, space group P212121, Z = 4]. Each unit cell includes 8 **neotame** and 12 MeOH mols. Disorder exists in one **neotame** mol. and one MeOH mol. The crystals were characterized by the following techniques: hot-stage microscopy (HSM), Karl-Fischer titrimetry (KFT), powder x-ray diffractometry (PXRD), differential scanning calorimetry (DSC), thermogravimetry (TGA), and 13C solid-state NMR (SSNMR). Under HSM at a heating rate of 10.degree./min, the sample melts at 64-84.degree. and liberates bubbles at 71-86.degree.. DSC in open pans shows two overlapping endotherms at 56 and 71.degree., probably due to melting and desolvation, resp. TGA in open pans shows 5.9% wt. loss due to desolvation below 70.degree.. Under 23 mmHg over P4010 at 23.degree.,

the

MeOH solvate produces pure amorphous **anhydrate**, which converts to cryst. **neotame**.H2O in the presence of moisture.

RE.CNT 21

RE

- (1) Andrew, E; Prog NMR Spec 1971, V8, P1 CAPLUS
 - (3) Anon; US 5728862 CAPLUS
 - (5) Blessing, R; Acta Crystallogr 1995, VA51, P33 CAPLUS
 - (6) Dixon, W; J Magn Res 1982, V49, P341 CAPLUS
 - (7) Goodman, M; J Peptide Sci 1998, V4, P229 CAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> logoff hold

COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
18.24	61.85

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
-2.35	-5.88

CA SUBSCRIBER PRICE

SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 08:51:33 ON 18 APR 2001